Behavioral and neuroimaging studies on language processing in Dutch speakers with Parkinson's disease

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Chapter 7
Distinct roles of the inferior frontal gyrus and basal ganglia in sentence comprehension in healthy subjects: an fMRI study

7.1 Introduction

A long tradition of aphasia studies have produced some major conclusions concerning language processing in the brain. First, the left hemisphere (LH) is the dominant hemisphere for language processing in most people, particularly right-handed individuals. Second, distinct peri-sylvian regions within the LH are involved in different aspects of language. Broca's area (Brodmann's area (BA) 44/45) is traditionally described as being involved in syntactic processing, whereas Wernicke's area (BA 22) is more involved in semantic processing. However, even though current imaging studies consistently show activation of Broca's and Wernicke's area during language tasks, this traditional view on language processing has been shown to be incomplete and therefore misleading.

Although the functional lateralization of language to the LH is confirmed by recent functional neuroimaging studies, the right hemisphere (RH) also has a significant contribution to language processing, in particular in lexical processing (Stowe et al., 2005) and in healthy aging. The right homologue of the left inferior frontal gyrus (LIFG) appeared to play a role in the comprehension of lexical semantic ambiguities, in which the right frontal lobe is involved in construction of a secondary interpretation of the sentence or revision of the initial interpretation (Stowe et al., 2005). This finding is in line with the higher activation of the RH compared to the LH during higher-level language tasks, such as comprehending metaphors (e.g., Mashal et al., 2005), jokes (e.g., Coulson and Wu, 2005) and repairing grammatical errors (Meyer et al., 2000). In addition, RH recruitment in the older participants included in this study (Mean= 57.3 years) is expected, since it might be possible that the contra-lateral homologue of LH language areas will be recruited due to diminished neural resources as a result of healthy aging (Cabeza, 2002). For these reasons the ROI analyses which we carried out included both the left and right IFG.

Furthermore, there is evidence against the purely cortical doctrine of language processing. Destruction of Broca's area or Wernicke's area can spare language function and only cause a transient form of aphasia, as long as subcortical white matter and basal ganglia (BG) are not damaged (Alexander et al., 1987; Stuss & Benson, 1986). This restoration of linguistic knowledge points to a distributed representation of linguistic knowledge in the human brain and to a vital participation of subcortical structures, like the BG, in language processing.

The neural circuits that link the subcortical BG and the frontal regions of the cortex are called the cortico-striato-cortical circuits (see Chapter 2 for a detailed description and Alexander et al., 1986; Middleton & Strick, 1994, 2000). The flow of information within these circuits is topographically organized from the cortex through the BG to the thalamus and back to the frontal cortex. Five different circuits were described by Alexander et al. (1986). In addition to these five circuits, in anatomical studies of non-human primates all frontal regions examined have been found to receive inputs from cortico-striato-cortical circuits (Middleton & Strick, 2002). By using Diffusion Tensor Imaging (DTI), Lehéricy et al. (2004) could demonstrate in a non-invasive way the existence of distinct cortico-striato-cortical circuits in humans that had till then only been hypothesized on the basis of primate-human extrapolations. It is not unlikely that the inferior frontal gyrus (IFG), which is known to be involved in sentence processing, also forms part of a circuit connected with the BG which is used while, for example, comprehending a sentence. Ullman (2006) hypothesized that Broca's area might be part of a neural circuit that links the frontal cortex to the BG. Along the same line, Chenery et al. (2008) supported the hypothesis that the LIFG, as part of a closed cortico-striato-cortical circuit, contributes to ambiguity processing. Recently Snijders et al. (2010) reported that the striatum was connected to LIFG for ambiguous sentences versus unambiguous sentences.

In the next section we will discuss the evidence for contributions of both the IFG and BG to particular aspects of language processing as well as evidence for dissociations between their roles in those processes.

7.1.1 The inferior frontal gyrus

First of all, various lines of evidence point to the involvement of the IFG in dealing with syntactic complexity. Sentences are defined as syntactically complex when the thematic roles (semantic interpretation within the sentence) are not in basic or canonical word order and therefore require extra grammatical operations. Simple syntactic structures (such as active sentences) can be distinguished from syntactically complex structures (such as passive sentences). Consider the following Dutch examples of an active sentence in (1) and passive sentence in (2), which are typical of the structures that have been employed in our study:

(1) Emma heeft de vlinder getekend
'Emma has the butterfly drawn'
(Emma has drawn the butterfly)

(2) De vlinder$_i$ wordt door Emma t$_i$ getekend
'The butterfly is by Emma drawn'
(The butterfly is drawn by Emma)

In the Dutch sentence in (1) and its literal English translation, the basic word order is subject-object-verb (SOV), with the subject (Emma) before the direct object (de vlinder *'the butterfly'*) and the main verb (getekend *'drawn'*). Hence, the agent (Emma) is in the subject position and the patient (de vlinder *'the butterfly'*) is in the direct object position.

However, in the more complex non-canonical sentences, such as the passive in (2), the noun phrases (NPs) and their thematic roles are not in their basic order (i.e., they have a non-canonical order).

The finding that syntactic processing depends on the LIFG is supported by evidence from Broca's aphasia, as pointed out in classic aphasia literature. Caramazza and Zurif (1976) were the first to observe difficulties with the comprehension of syntactically complex sentences in individuals with Broca's aphasia. The Broca's aphasic individuals in their study made more errors on a sentence comprehension task when the sentence item involved the reversal of the NPs to which agent and patient thematic roles were assigned.

Many blood-flow based [i.e., functional magnetic resonance imaging (fMRI) and positron emission tomography (PET)] studies have investigated the effects of syntactic complexity, showing that for the processing of syntactically complex sentences, mainly the LIFG, the left middle/superior temporal gyrus (MTG/STG) and their right homologue areas were activated (e.g., Constable et al., 2004; Cooke et al., 2002; Friederici et al., 2006; Just et al., 1996; Peelle et al., 2004; Stromswold et al., 1996).

The IFG has also been closely linked to processing of grammatical violations. Grammatical violations have most typically been used in Event Related Potential (ERP) studies. In ERP studies, participants frequently read or hear correct sentences mixed with sentences that contain a violation of the semantics or syntax of the sentence. Syntactic violations generally elicit left-lateralized early negativities on electrodes over anterior cortex or sites [(early) left-anterior negativity or (E)LAN] and later positivities on electrodes over centro-parietal regions (P600), while semantically ill-formed sentences elicit negativities (N400) which are also distributed over more posterior scalp.

In the present study, two types of grammatical violations were used. The first type was a violation of the morphosyntactic relation between the auxiliary and past participle of the main verb as illustrated in the Dutch sentence (3):

(3) Emma heeft de vlinder <u>getekend</u>
* Emma heeft de vlinder <u>tekent</u>
' Emma has the butterfly <u>draws</u>'*
(Emma has draws the butterfly)*

Morphosyntactic violations such as the inflectional violation used in the present study elicit a LAN effect occurring between 300 and 500 ms (Gross et al., 1998; Gunter et al., 2000; Hahne & Jescheniak, 2001; Penke et al., 1997; Vos et al., 2001). It has been suggested that the (E)LAN reflects highly automatic first-pass parsing processes (Friederici, 1995, 2002; Hagoort, 2003; Hahne & Friederici, 1999), which are already present during early language development (Oberecker et al., 2005). The P600 is a syntactic late positivity that is more under the control of attention and occurs between 500 and 1200 ms. The P600 is seen as an effect of secondary syntactic processes such as reanalysis and repair (Friederici & Mecklinger, 1996).

The second type of violation used in the present study was a violation of the verb-argument structure that violates both the syntactic and semantic aspects of sentence processing. The Dutch example in (4) illustrates that the intransitive verb *niezen* 'to sneeze' can only entail one argument, an agent, and thus cannot take a patient.

(4) Emma heeft de vlinder getekend
* Emma heeft de vlinder geniesd
' Emma has the butterfly sneezed'*
(Emma has sneezed the butterfly)*

Thus if niezen *'to sneeze'* is contained in a sentence with two arguments (an agent and a patient), the sentence is grammatically incorrect. In this type of violation, the sentence-final verb cannot be integrated with the preceding argument information. Simultaneously, the sentence is also semantically violated, because there is no semantic interpretation for the butterfly in this sentence. An ERP study conducted in German by Friederici and Frisch (2000) used sentences with this second type of violation. The authors found that this argument-structure mismatch on the basis of the number of arguments elicits a compound waveform with a negative (N400) and positive (P600) peak. Friederici and Frisch (2000) claimed that the presence of the extra direct object influences processes at the level of lexical-semantic integration, which is seen in the signal as a N400 component. The P600 was seen as an effect of the repair processes following the disturbed lexical-semantic integration.

Several neuroimaging studies have confirmed the involvement of the IFG in syntactic violation processing (Kuperberg et al., 2000, 2003; Moro et al., 2001; Newman, et al., 2001; Newman, et al., 2003; Ni et al., 2000; Raettig et al., 2010; Ruschemeyer et al., 2005). The results are quite varied, however, probably due to differences in materials, languages and tasks, but they do support the results from the ERP studies.

Most relevant to the current study, a study in German reports on both violation types that are also under investigation in the present study. Differing from the current study, the violations in this German study were presented auditorily and were limited to passive sentences (Raettig, Frisch, Friederici, & Kotz, 2010). The first type of violated sentences contained a morphosyntactic mismatch between the auxiliary and the main verb [e.g., *Im Haus wurde bald streichen und renoviert, **'In the house was soon painted and renovated'*]. This inflectional violation elicited an increase in brain activity in the left MTG to posterior STG. Their second violation, a verb-argument structure violation [e.g., *Das Konzert wurde bald gehustet und unterbrochen, **'The concert was soon coughed and disturbed'*], is comparable to the violation described in Friederici and Frisch (2000) and elicited brain activations in the left IFG (BA 44).

Although the IFG is clearly involved in some aspect of sentence processing, there has been considerable discussion on its exact role. Some more specific models on LIFG function have also been suggested on the basis of findings in neuroimaging studies. The Memory, Unification, and Control model, proposed by Hagoort and colleagues (Hagoort, 2003, 2005; Hagoort et al., 2004), assumes that the LIFG is involved in combining retrieved information into larger units (i.e., unification). Furthermore, Hagoort (2005) hypothesized that the LIFG holds an anterior-ventral to posterior-dorsal gradient for unification, such that BA 47 and BA 45 are involved in semantic processing and BA 45 and 44 contribute to syntactic processing.

Similarly, Friederici (2002) stated that semantic integration within a sentence takes place in the left BA 45/47 and morphosyntactic integration in the left BA 44/45. In order to investigate whether distinct subregions within the IFG contribute differentially to sentence processing, all three IFG subregions were included in the region of interest (ROI) analysis of the present study. The regions of the IFG involve the pars opercularis (BA 44), the pars triangularis (BA 45) and the pars orbitalis (BA 47).

7.1.2 The basal ganglia

Importantly for the current study, there is evidence that the BG contribute to both syntactic complexity and violation processing. The neuroimaging study of Crosson et al. (2003) provided evidence for the involvement of the BG in lexical processes. According to Crosson et al. (2003), BG have the function of maintaining a bias towards a lexical item chosen from among others in competition during controlled word generation. However, there is little supporting evidence from neuroimaging studies for the involvement of the BG in the processing of syntactic complexity. However, several studies on degenerative disorders of the BG such as Parkinson's disease (PD) have provided evidence for the involvement of the BG in the processing of syntactic complexity. These studies demonstrated that non-canonical structures, such as passives, and sentences with object-gap subordinate clauses, were most vulnerable in individuals with PD (see Grossman, 1999; Murray, 2008 for an extensive review). For this reason, we will focus on the BG by carrying out a ROI analysis on the processing of non-canonical passives in the BG.

Turning to violation processing, ERP studies in BG-lesioned patients revealed an intact early left anterior negativity (ELAN), but no P600 effect in patients with lesions in the left BG (Friederici et al., 1999; Frisch et al., 2003; Kotz & Friederici, 2003; Kotz et al., 2003). Additionally, other ERP studies by the Friederici research group have shown that neurodegeneration of the BG due to PD influences the language-related ERP components dramatically. In a study by Kotz et al. (2002), the eight PD patients included showed an intact ELAN, but strongly reduced P600. In another study, Friederici et al. (2003) compared PD patients to controls. As predicted, the PD patients showed an intact ELAN and a reduced P600. According to Friederici et al. (2003), the alteration in the P600 reflected distortions of the late controlled syntactic integration processes in PD. The reduction in PD patients' P600 amplitude might point to a lack of integrity of the cortico-striato-cortical circuits responsible for its generation. Thus, the left frontal cortex and the left anterior temporal cortex contribute together to the early automatic processing underlying the (E)LAN, whereas the left BG contribute to the late controlled syntactic integration processes underlying the P600, as evidenced by the reduction of the P600 effect in patients with focal BG lesions or PD (Friederici & Kotz, 2003; Friederici et al., 2003). On the basis of the patient studies described above it might be concluded that the frontal cortex and the BG are differently involved in sentence processing, at least in regard to the processing of violations.

A number of fMRI studies in healthy participants (e.g., Moro et al., 2001, Ni et al., 2000) have also implicated the BG [particularly the caudate nucleus (Caud)] in the processing of grammatical violations.

A final consideration is which area within the BG may be involved in these processes. Involvement of the BG in cognitive functioning is not limited to the striatum. According to Owen et al. (1998), the cognitive impairments in PD are due to disturbed BG outflow, particularly of the right globus pallidus, which has in turn an impact on the information transfer to the frontal cortex. For the BG, we choose therefore, to include both input nuclei [i.e., Caud and putamen (Put)] and principal output nuclei [i.e., globus pallidus or pallidum (GP)] of the cortico-striato-cortical circuit in the ROI analysis.

The goal of the current study is to investigate 1) the extent to which the IFG and the BG collaborate on two aspects of sentence processing: dealing with non-canonical structures and violations, and 2) the extent to which they appear to play similar or different roles during the processing of these language phenomena. To achieve this goal we carried out an fMRI study which was analyzed using ROIs in the IFG and the BG bilaterally. In addition a whole-brain analysis was carried out to identify any additional areas that might be prominently involved.

7.2 Materials and methods

7.2.1 Subjects

Sixteen healthy subjects recruited from the Groningen community participated in this study. Participants were screened for any history of neurological or psychiatric conditions prior to inclusion. Exclusion criteria were dementia (Mini-Mental State Examination (MMSE) < 25; Folstein, Folstein, & McHugh, 1975) and depression (Montgomery-Åsberg Depression Rating Scale (MADRS); Montgomery & Åsberg, 1979) ≥ 18 (Leentjens et al., 2000). All subjects were native speakers of Dutch, who reported no language difficulties (such as dyslexia) and had self-reported normal or corrected-to-normal vision. One participant was excluded from further analyses due to movement artifacts. Data from the remaining 15 participants (6 female; mean age = 57.3 years, range = 45-69 years) were analyzed. Handedness was determined using the Dutch version of the Edinburgh Handedness Inventory (Van Strien, 1992); all participants were strongly right-handed.

This study was approved by the Medical Ethical Committee of the University Medical Center Groningen (UMCG). All participants gave their written informed consent according to the Declaration of Helsinki. The subjects were checked for absence of bodily ferromagnetic materials and other MRI incompatibility. During scanning, the standard MRI safety regulations were followed.

7.2.2 Stimulus material

In the experiment two within-subject factors were crossed in a 2x3 factorial design resulting in six experimental conditions. The first factor was 'canonicity' with two levels: active and passive voice. The second factor was 'grammaticality' with three levels: no violation, inflectional violation, and violation of the verb-argument structure. 120 transitive verbs, 120 intransitive verbs and 240 nouns were selected to construct the experimental sentences.

The 240 critical verbs and the 240 nouns used in the final experimental sentences were controlled for lemma frequency and word length. The frequency counts were based on the Dutch CELEX corpus (Baayen et al., 1993). The characteristics of the verbs and nouns are summarized in Table 7.1.

Table 7.1: Characteristics of the critical verbs and nouns used in the experimental sentences [Mean (SD)] per condition

Condition	*Word class*	*n*	*Verb inflection*	*Transitivity*	*Number of letters*	*Frequency*
AN and PN	Verb	240	participle	Transitive	7.77 (1.43)	.80 (.60)
AI and PI	Verb	240	3rd person singular	Transitive	5.82 (1.42)	.80 (.60)
A-VA and P-VA	Verb	240	participle	Intransitive	7.95 (1.32)	.79 (.53)
All conditions	Noun	240	n/a	n/a	7.13 (1.99)	1.19 (.60)

Note: For the abbreviations see List of Abbreviations.

In Table 7.2 examples of experimental sentences are given. All non-violated active sentences (AN) consisted of a first NP, made up of a definite article (de, het) and a singular [+human] noun, the finite form of the auxiliary verb hebben *'to have'*, i.e., heeft *'has'*, a second NP and the past participle of a target verb. The verbs of the active sentences were used to construct the passive sentences. In order to avoid a repetition effect, the agent and patient nouns were changed. Thus, the non-violated passive sentences (PN) consisted of a first NP, the finite form of the auxiliary verb worden *'to be'*, wordt *'is'*, a prepositional phrase (PP) containing the preposition *door* 'by' and a second NP, and the past participle of the same critical verb as in the active condition. The sentences were semantically reversible, meaning that no semantic knowledge could be used to interpret the sentences.

The violated sentences were constructed by replacing the critical verb in sentence final position. It was either replaced by the 3rd person singular (to avoid ambiguity concerning the word category) in the inflectional violation condition (AI or PI) or by the past participle of an intransitive verb in the violation of the verb-argument structure condition (A-VA or P-VA).

In both the violated and the correct sentences, the target verb was not strongly associated with the preceding NP arguments, although the combination of words was always semantically plausible: for example 'to tip someone off' is semantically not strongly associated with either *'the jeweler'* or *'the poulterer',* but it is semantically plausible (see example sentence Table 7.2). In the correct sentences (no violation) and the violation of the verb-argument structure condition, the past participle of the verbs placed in sentence final position always started with the regular Dutch participial morpheme ge-.

In order to control whether the sentence materials activated the classical language regions, including inferior frontal and temporal regions, we developed a visual control condition consisting of 120 Consonant Strings (CS). In Table 7.2 examples of CS are also given.

Table 7.2: Examples of the experimental materials in Dutch

Grammaticality	***Canonicity***	
	Active	Passive
N	De juwelier/ heeft/ de poelier/ <u>getipt.</u> *The jeweler has the poulterer tipped off.*	De pater/ wordt door/ de militair/ <u>getipt.</u> *The father is by the soldier tipped off.*
I	De juwelier/ heeft/ de poelier/ <u>tipt.</u> *The jeweler has the poulterer tips off.*	De pater/ wordt door/ de militair/ <u>tipt.</u> *The father is by the soldier tips off.*
VA	De juwelier/ heeft/ de poelier/ <u>geproest.</u> *The jeweler has the poulterer snorted.*	De pater/ wordt door/ de militair/ <u>geproest.</u> *The father is by the soldier snorted.*
CS	Vm gthsv/ kcrtf/ pg btcpkh/ bcpfhsvhn.	Vm mglbsfv/ vsntf hmcg/ pg vbntjsg/ kjgpfvbgsd.

Note: The accompanying literal English translation is given. Each segment border is indicated with a vertical line.
See for the abbreviations in the List of Abbreviations.

Plausibility and grammaticality of the sentences were evaluated separately using off-line preratings by 184 (127 female; mean age = 21.3 years, range = 19-30 years) and 90 (71 female; mean age = 20.3 years, range = 18-30 years) Dutch-speaking healthy volunteers respectively. All volunteers were undergraduate students from the University of Groningen. None of them participated in the fMRI or behavioral experiment afterwards.

Plausibility of sentence content was determined by judging the grammatically correct sentences only, using a seven-point rating scale (1=totally implausible and 7= seeming reasonable or probable). Sentences with a plausibility rating of less than three were equally distributed across the experimental stimuli lists (see below). The off-line plausibility ratings of the base item for each of the experimental conditions are summarized in Table 7.3 A. The average plausibility ratings of the materials per condition were intermediate, but still sufficient.

The grammaticality of the items was tested on the passive sentence structures only. Students could judge the sentences as being either correct or incorrect. Table 7.3 B summarizes the descriptive statistics. According to the Friedman's ANOVA, the judgments differed significantly ($\chi^2_{(2)} = 225$; $p < .05$). Subsequently, Wilcoxon tests were used to follow up this finding. A Bonferroni correction was applied and therefore the effects were reported at a .025 level of significance. The non-violated sentences were interpreted as more grammatical than the sentences with an inflectional violation (W = 7260; $p < .025$) or a violation of the verb-argument structure (W = 7298; $p < .025$).

Table 7.3 A: Plausibility of the test materials per condition

Condition	*n*	*Plausibility rating [Mean (SD)] (1-7; 7= totally plausible)*
AN	120	4.64 (1.05)
PN	120	4.86 (1.09)
AI	120	4.64 (1.05)
PI	120	4.86 (1.09)
A-VA	120	5.15 (1.02)
P-VA	120	5.26 (.88)

Note: For abbreviations see List of Abbreviations

Table 7.3 B: Grammaticality of the test materials per condition

Condition	*n*	**Grammaticality judgement** [Mean (SD)]
PN	120	.84 (.19)
PI	120	.02 (.04)
P-VA	120	.10 (.11)

Note: For abbreviations see List of Abbreviations

Ninety filler sentences were added to the lists in order to present more correct than incorrect stimuli (so as not to attract the attention to the violations) and also to vary the timing within the blocks of sentences during the fMRI scanning. The filler sentences contained 70 intransitive verbs and 20 transitive verbs that can be inflected with either the auxiliary hebben *'to have'* or zijn *'to be'*. Five different types of filler sentences were developed according to the timing of the segments. Table 7.4 illustrates all the filler sentences per type. Four of the filler types were in the active voice and took an intransitive verb. Only filler type 5 was in the passive voice and was created with a transitive verb. Filler type 4 and 5 contained an adverb as an extra segment.

Table 7.4: Examples of filler sentences per type

Filler type	n	Sentence
1	20	Hij/ is/ snel/ gesprongen. *He has quickly jumped*
2	15	De jongen/ is/ met hem/ gesprongen. *The boy has together with him jumped*
3	15	De jongen/ is/ met het meisje/ gesprongen. *The boy has with the girl jumped*
4	20	De jongen/ is/ met hem/ snel/ gesprongen. *The boy has with him quickly jumped*
5	20	De jongen/ wordt/ door het meisje/ hard/ geduwd. *The boy is by the girl hardly pushed*

Note: The accompanying literal English translation is given. Each segment border is indicated with a vertical line.

To avoid repetition effects, the final 720 experimental sentences were divided into three different lists (with 40 sentences of each of the six conditions per list), so that participants saw only one version of each sentence set (no violation, inflectional violation or violation of the verb-argument structure) but an equal number of sentences in each condition. Each list of 240 experimental sentences was completed with the same 90 filler sentences and 120 CS. The order of the sentences within a list was pseudo-randomized and then kept constant. A block of sentences always started with two filler sentences, after which two sentences of each condition and two or three extra filler sentences followed in a randomized order. However, no more than two items of the same condition were presented consecutively within a sentence block.

7.2.3 Experimental procedure

A mixed block/event related fMRI design was used. The blocks contrasted sentence reading and visual processing of CS. The different sentence conditions were presented in pseudo-random order within sentence blocks in an event related design to avoid the predictability of the next upcoming trial typical for pure block designs. From ERP studies we know that predictability influences the effects of the violations (Coulson et al., 1998; Gunter et al., 1997; Hahne & Friederici, 1999).

The participants were instructed to read the sentences carefully. During the experiment, each participant was presented with one list of experimental trials separated in four runs (circa 11 minutes per run). Each run contained five blocks of sentences and six blocks of visual controls. A sentence block took between 88 sec (four fillers) and 92 sec (five fillers) and a visual control block always took 34 sec.

To avoid eliciting abnormal strategies, especially to the violations, participants were asked simply to read the sentences for comprehension rather than making any judgment. To check if participants' attention remained focused on reading the sentences, they were asked to press a button with the right hand as soon as they detected a star on the screen. Every sentence and visual control block started with this visual cue, followed by a button press.

Each experimental trial was presented visually in a sequence of four (or five) segments. Segmentation of the experimental sentences, the CS and the filler sentences is indicated in Tables 7.2 and 7.4. Experimental presentation and response collection was conducted using the E-prime software program (Psychology Software Tools Inc., 2001). The segments were projected on the central portion of the screen and could be seen by the participants in the magnet through a system of mirrors. The letters were printed in black on a grey background and following the normal case rules of Dutch orthography. The end of a sentence was marked with a full stop. The segments were presented either for 400 msec when containing one word or for 800 msec when containing two or three words. All experimental trials began with the presentation of a cross as a fixation point in the center of the screen and ended with a fixation cross for 100 msec. The duration of the fixation cross at the beginning of a visual control trial was always 2900 msec. The mean duration of the fixation cross of the sentence trials was 3000 msec and ranged between 2000 msec and 5000 msec to make sure that every presentation of the fourth segment, containing the target verb, was presented at a slightly different phase of the scanning cycle (jittering).

Each participant completed a short practice session before entering the scanner. This was done using a laptop computer to display the practice trials, while instructions were given verbally.

7.2.4 Image acquisition

Functional and anatomical images were collected using a 3T Philips MR system (Best, The Netherlands) with an 8-channel sense head coil. Foam padding and a forehead strap were used to restrict head motion. Anatomical images were collected (TR = 25 msec, TE = 46 msec[19], flip angle = 90°, slices = 160, isotropic voxels 1x1x1 mm, axial orientation) in between run 2 and 3.

Functional images using the BOLD contrast (TR = 3000 msec, TE = 30 msec, flip angle = 80°, slices = 47, isotropic voxels 2.5x2.5x2.5 mm, axial orientation) were collected while participants performed the experimental task. A total of 924 functional volumes were collected (ranging from 230 to 232 per run).

7.2.5 Data analysis

The raw fMRI data were converted into analyze format using the MRIcro software package (Rorden & Brett, 2000). Next, data were processed and analyzed using Statistical Parametric Mapping version 5 (SPM5) operating on a MatLab platform (www.fil.ion.ucl.ac.uk/spm/software/spm5). Preprocessing steps with SPM5 included within-subject realignment, co-registration of the mean BOLD image with the structural image, and spatial normalization of the structural image to the template of Montreal Neurological Institute (MNI) average brain. Images were smoothed using a Gaussian kernel of 8 mm full-width half-maximum (FWHM). The realigned data were evaluated according to movement artifacts criteria formulated in advance. Participants showing movements within a run of trials that parallels the button push were excluded. Furthermore, if between or within runs

[19] TR represents repetition time and TE is echo time.

translation movements exceeded 4 mm and rotation movements exceeded 3 degrees, participants were also excluded. Under these criteria, the data of one participant were omitted.

Statistical analyses were performed on individual and group level using the General Linear Model (GLM) as implemented in SPM 5. For the statistical model a matrix including all conditions and an implicit baseline was built. Each sentence was modeled both for its full duration and for the onsets of the critical verb segment. Similarly the full duration of the CS and the onset of the fourth segment were modeled.

Region of interest (ROI) analysis

As described in the Introduction section, the aim of the study was investigating the involvement of circuits when participants read sentence materials in which the variables of canonicity and grammaticality were crossed. Therefore, six planned ROI's were analyzed bilaterally.

1. Caudate nucleus (Caud)
2. Putamen (Put)
3. Globus pallidus (GP) or pallidum
4. BA 44 or pars opercularis of the IFG
5. BA 45 or pars triangularis of the IFG
6. BA 47 or pars orbitalis of the IFG

ROI definition and signal extraction was performed using MARSBAR (Brett et al., 2002). These ROIs were defined anatomically using the Anatomical Automatic Labeling (AAL) map of the MNI brain (Tzourio-Mazoyer et al., 2002). For all the ROIs average activation values per condition were extracted for each participant. Further statistical analyses were done using the Statistical Package for the Social Sciences version 16 (SPSS 16.0). First, the raw data extracted for each anatomical ROI were transformed into z-values. Secondly, normality of the distribution of the z-values was analyzed with the Kolmogorov-Smirnov Test separately for each ROI area and for each separate condition. All variables were found to be normally distributed. Third, if sphericity was violated, a correction factor was used to adept the degrees of freedom for the test, reducing the significance level to a more accurate number. SPSS provides Mauchly's Test of Sphericity and its significance. If the assumption of sphericity was violated, the output for the Greenhouse-Geisser correction factor was interpreted. Finally, a series of repeated measures (2x2x3) ANOVAs with the factors hemisphere (LH and RH), canonicity (active and passive) and grammaticality (no violation, inflectional violation and violation of the verb-argument structure) were performed.

Whole brain analysis

At the first level, individual subject analyses specifying contrasts between reading of the full sentences and viewing whole CS were calculated. The contrast-images (difference in β estimates) of the first-level analysis were then used for the second-level group statistics. Significance was judged at the voxel level ($p < .001$, uncorrected) and by a cluster size of 20 ($p < .05$, corrected for multiple comparisons). A one sample t-test was used to determine the areas that responded more strongly to sentences as compared to looking at CS for the whole sequence duration. The statistical parametric maps (SPM $\{T_{14}\}$) were thresholded at $T \geq 3.79$.

A factorial design matrix was applied to test the main effect of canonicity, the main effect of grammaticality and the interaction effect. For each participant, at the first level, six contrasts were generated by contrasting the activation of the critical verb segment of each of the six conditions with the activation of viewing the fourth segment of the CS. The main effect of canonicity (two levels) was tested using a t-test. The statistical parametric maps (SPM $\{T_{70}\}$) were thresholded at $T \geq 3.21$. Subsequently, an F-test was used for the main effect of grammaticality (three levels) and for the interaction effect grammaticality x canonicity. The relative contribution of each violation condition to the main effect of grammaticality and interactions with canonicity was examined by post hoc analyses on the mean signal change in ROIs described above. In both cases, the statistical parametric maps (SPM $\{F_{2,70}\}$) were thresholded at $F \geq 7.64$.

In general, the maxima of suprathreshold regions were reported in MNI coordinates as used in SPM5. Brain regions were identified using MRIcroN software (www.sph.sc.edu/comd/rorden/mricron). In separate tables, the anatomical description and the corresponding BAs were also reported.

7.2.6 Behavioral testing

After the scanning procedure, all participants were tested with a violation detection task. The stimuli used during the violation detection task were similar to the materials used during the fMRI scanning task. An additional prepositional phrase followed the last segment of the original fMRI sentences to give participants time to respond. Thus, all the sentences in the behavioral study consisted of five segments. The sentences were presented segment by segment. A trial started with the presentation of a fixation cross at the center of the screen for 450 msec, followed by the first segment. Each one-word segment appeared on the screen for 400 msec and each two-word segment for 800 msec. A 750 msec blank screen followed the last word of the sentence. After the blank screen a question mark appeared only if the participant did not press the red button while reading the sentence. We measured the Reaction Time (RT) of the response between the onset of the segment with a violation and the actual button press. Also the accuracy of the response was measured. Each participant judged a list consisting of 90 sentences, of which 36 were test sentences (six of each of the six experimental conditions). The other 54 sentences were distracters, 30 of these distracters were anomalous on a different segment than the lexical verb and 24 were normal sentences. The participants were assigned to one of the two lists of items that she/he did not see in the fMRI scanner.

Experimental presentation and response collection was conducted using the E-prime software (Psychology Software Tools Inc., 2001). The participants were instructed to read the written sentences on the screen of a laptop and to judge if a given sentence made sense. The participants were asked to press a red button on the keyboard of the laptop as soon as a sentence stopped making sense. Participants had to press a green button on the keyboard at a sentence final prompt (a question mark) if no error was encountered. Participants were asked to respond as quickly and accurately as possible when a violation was encountered and to wait for the question mark to affirm that the sentences was correct. The participants started the beginning of each new trial by pressing the space bar. Prior to the behavioral experiment, a practice session was conducted on correct and violated sentences.

To analyze the accuracy data, a repeated measures (2x2x3) ANOVA with the factors canonicity (active and passive) and grammaticality (no violation, inflectional violation and violation of the verb-argument structure) was performed. Many participants failed to react within the allowed response time, which was treated as a missing value in the data set and resulted in unreliable RTs (not a normal distribution). Therefore, a Friedman test was used on the RT data to evaluate the effects of canonicity and grammaticality. When the Friedman test was significant, pairwise comparisons between the different conditions were done, based on the Wilcoxon test.

7.3 Results

7.3.1 Behavioral results

There were no significant differences in the participants' accuracy scores for the different sentence types. For the latency data, Friedman's test showed no significant differences. Table 7.5 summarizes the descriptive statistics of the accuracy and latency data.

Table 7.5: Mean (SD) accuracy and latency to respond to stimuli during behavioral task

Sentence condition	Mean (SD) % correct	Mean (SD) msec latency
AN	94.44 (12.06)	568.08 (138.48)
PN	91.11 (8.61)	713.25 (366.16)
AI	92.22 (15.26)	989.58 (334.82)
PI	95.56 (11.73)	966.83 (322.44)
A-VA	84.44 (22.24)	1169.25 (474.35)
P-VA	85.56 (30.12)	1485.17 (80.14)

Note: For abbreviations see List of Abbreviations

The descriptive results of the latency data showed an order of processing time, indicating that the detection of a violation of the verb-argument structure in a passive sentence required the most time and that the active sentences without a violation were understood relatively fast.

7.3.2 Region of interest (ROI) analysis

Within each ROI, a (2x2x3) ANOVA with factors hemisphere x canonicity x grammaticality was conducted. The results for the BG and the IFG regions will be discussed separately.

Basal ganglia

For *the Caud* and *the Put*, the analysis revealed no significant effects. The *GP* showed a main effect of canonicity ($F_{(1, 14)} = 4.82$; $p < .05$) and an interaction effect of hemisphere x canonicity ($F_{(1, 14)} = 4.72$; $p < .05$). Subsequently, for each hemisphere separately, (2x3) ANOVAs with factors canonicity x grammaticality were performed. For the *left GP* no effects were evident. However, the ANOVA for the *right GP* revealed a main effect of canonicity

($F_{(1, 14)} = 8.42$; $p < .05$). As illustrated in Figure 7.1, more activation was found for the active sentences as compared to the passive sentences ($t_{(14)} = 2.90$, $p < .05$).

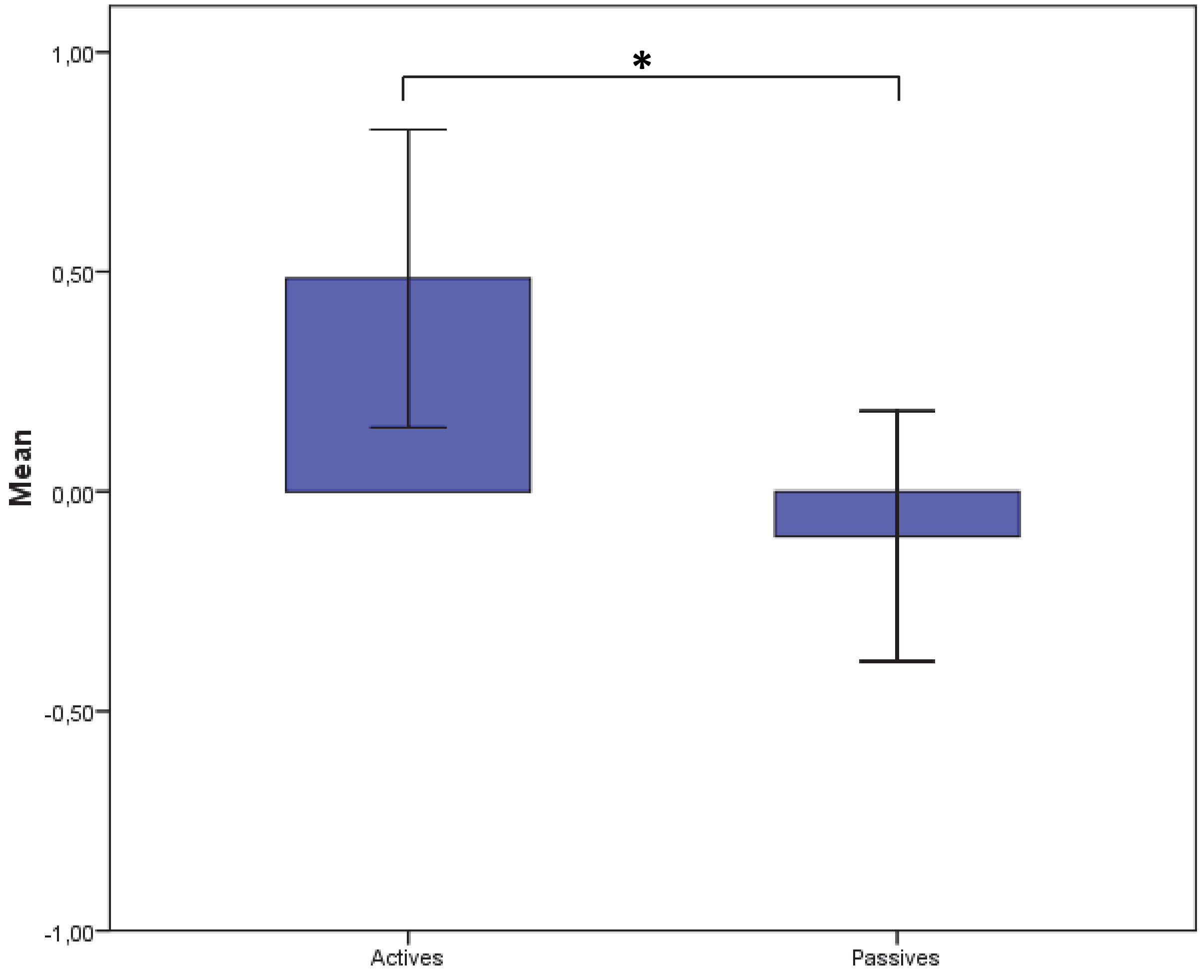
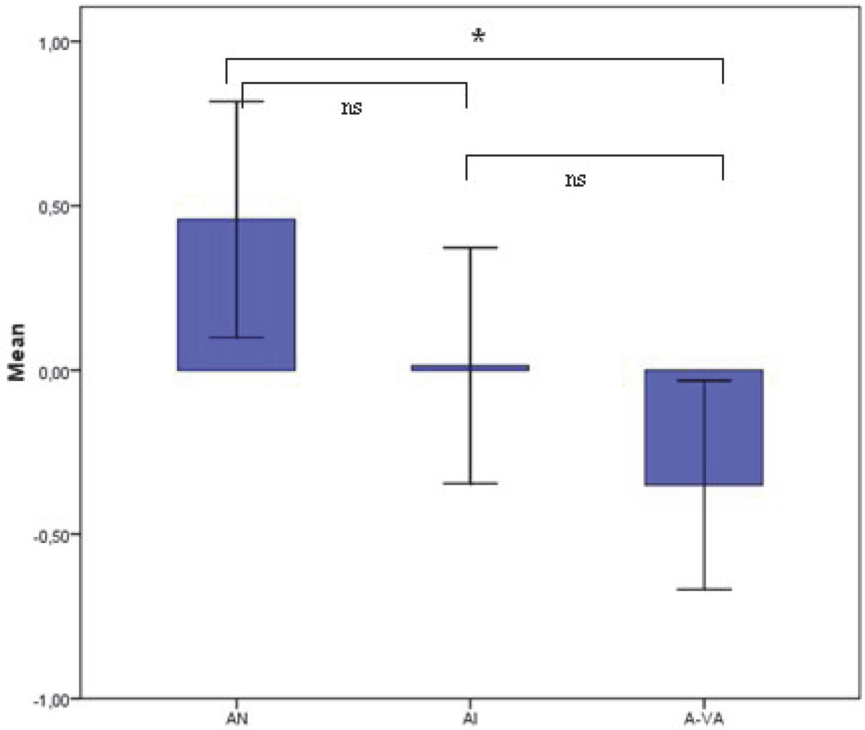


Figure 7.1: Mean activation in the right GP for active and passive sentences. Error bars indicate the standard error of the mean. * = $p < .05$.

Inferior frontal gyrus

For the *IFG pars opercularis* (BA 44), a significant interaction between canonicity and grammaticality ($F_{(2, 28)} = 5.14$; $p < .05$) was found. Figure 7.2 A and B illustrate that the participants recruited the bilateral BA 44 more for the active non-violated sentences compared to the passive non-violated sentences ($t_{(14)} = 3.12$, $p < .01$). Conversely, the sentences containing a violation of the verb-argument structure tended to activate the bilateral BA 44 more if the sentence was in the passive voice as compared to the active voice ($t_{(14)} = -2.02$, $p > .05$).

A



B

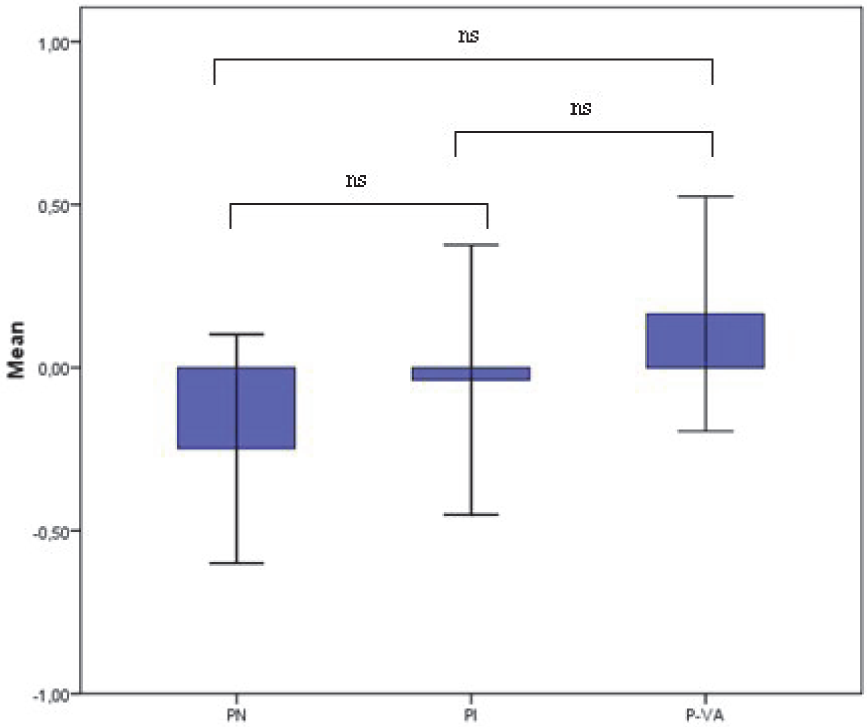


Figure 7.2: Mean activation for the bilateral IFG pars opercularis (BA 44) for A: the active sentences per violation condition and B: the passive sentences per violation condition. *Note:* For abbreviations see List of Abbreviations.

Within the active sentences, post hoc Least Significant Differences (LSD) pairwise comparison of the different violation types revealed that the non-violated sentences showed a significantly greater activation in the BA 44 compared to the sentences with aviolation of the verb-argument structure ($p < .05$), but not compared to the sentences with an inflectional violation. Sentences with an inflectional violation did not differ from sentences with a violation of the verb-argument structure (see Figure 7.2 A). However, within the passive sentences, post hoc LSD pairwise comparisons were not significant (see Figure 7.2 B).

For the nearby *IFG pars triangularis* (BA 45), the global (2x2x3) ANOVA showed a trend to a main effect of grammaticality ($F_{(2, 28)} = 3.19$; $p > .05$), an interaction of hemisphere x grammaticality ($F_{(2, 28)} = 3.50$; $p < .05$) and an interaction of canonicity x grammaticality ($F_{(2, 28)} = 4.57$; $p < .05$). Figure 7.3 A illustrates the results of the post hoc LSD pairwise comparison of the different violation types within the active sentences, in which the non-violated sentences showed a significantly greater activation in the BA 45 compared to the sentences with an inflectional violation ($p < .05$) and compared to the sentences with a violation of the verb-argument structure ($p \leq .001$). Again the post hoc LSD pairwise comparisons for the passive sentences were not significant (see Figure 7.3 B).

A

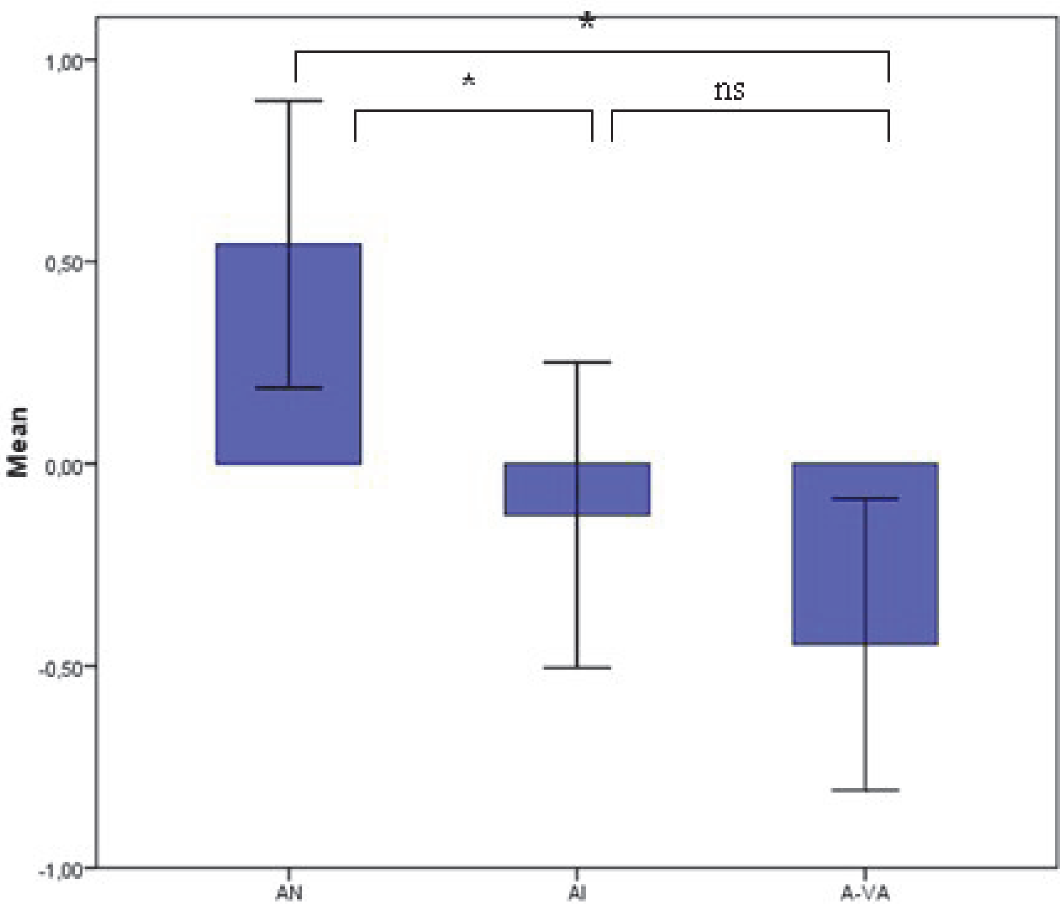


Figure 7.3: Mean activation for left and right IFG pars triangularis (BA 45) for A: the active sentences per violation condition. * = $p < .05$. Error bars indicate the standard error of the mean.
Note: For abbreviations see List of Abbreviations.

B

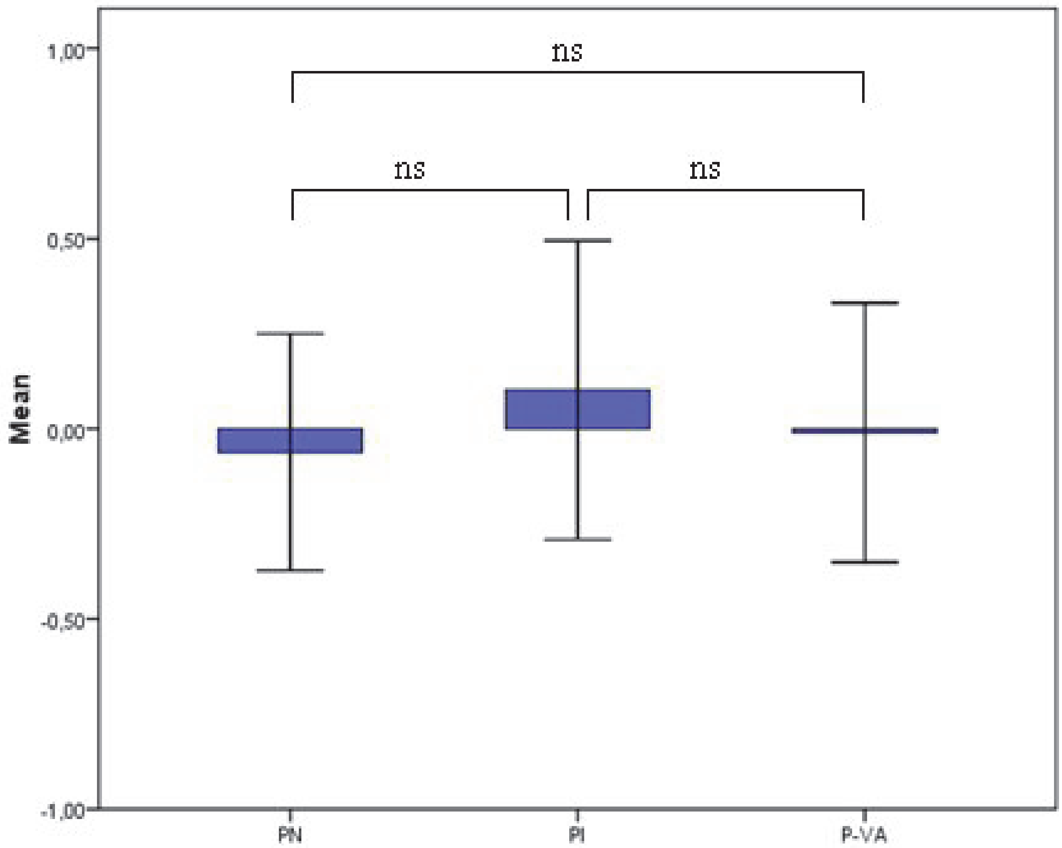
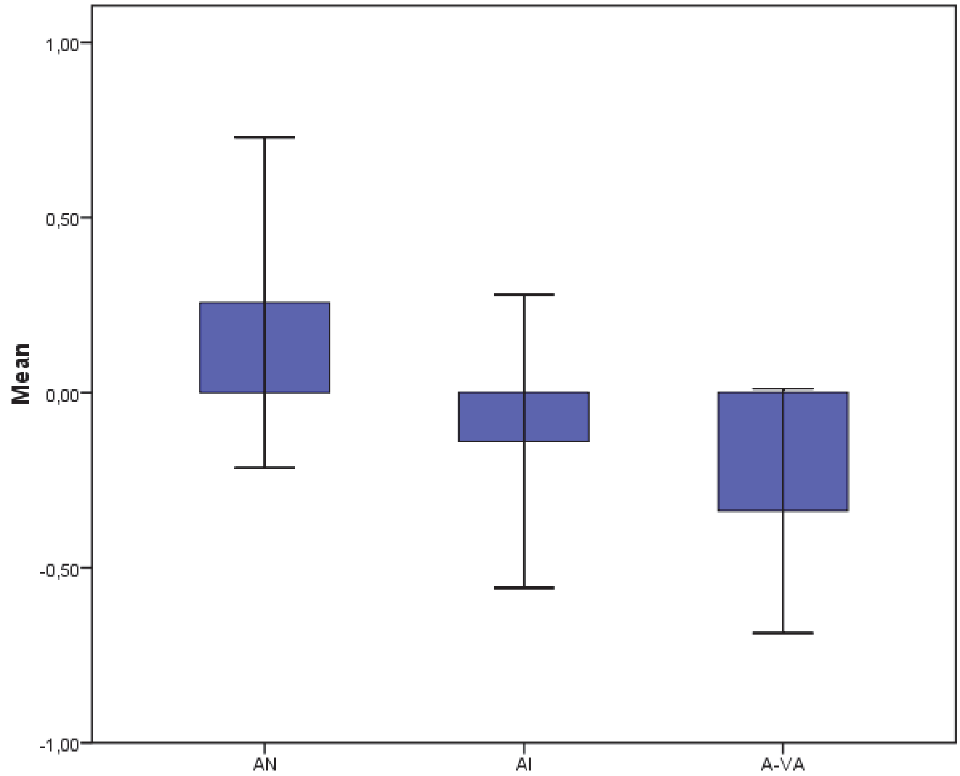


Figure 7.3: Mean activation for left and right IFG pars triangularis (BA 45) for B: the passive sentences per violation condition. Error bars indicate the standard error of the mean.
Note: For abbreviations see List of Abbreviations.

The post hoc repeated measure (2x3) ANOVAs with factors canonicity x grammaticality performed for the two hemispheres separately exposed a main effect of grammaticality ($F_{(2, 28)} = 6.05$; $p < .01$) for the BA 45, together with a trend to an interaction effect of canonicity x grammaticality ($F_{(2, 28)} = 2.99$; $p > .05$). Also in the BA 45 a marginal interaction effect of canonicity x grammaticality was evident ($F_{(2, 28)} = 3.17$; $p > .05$) .

Finally, for the *IFG pars orbitalis* (BA 47) only a trend to a grammaticality effect ($F_{(2,28)}= 2.73$; $p > .05$) was evident (see Figure 7.4 A and B). Thus no post hoc pairwise comparisons were conducted.

A



B

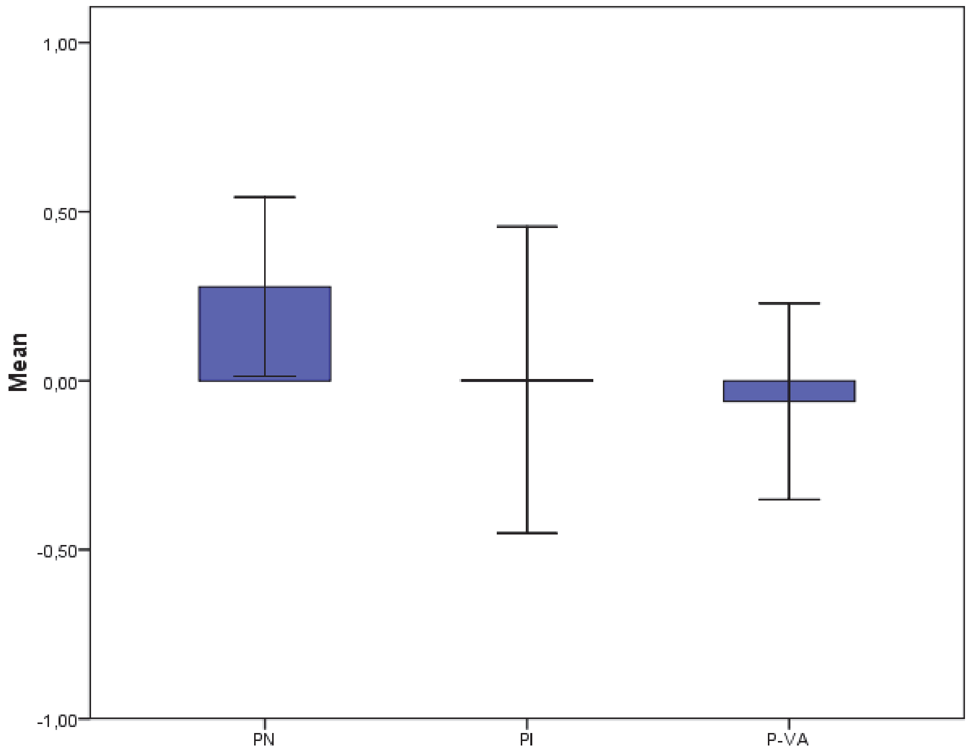


Figure 7.4: Mean activation for the bilateral IFG pars orbitalis (BA 47) for A: the active sentences per violation condition and B: the passive sentences per violation condition. Error bars indicate the standard error of the mean.

Note: For abbreviations see List of Abbreviations.

7.3.3 Whole brain analysis

When contrasted with the CS, reading of the sentences (whole sentence duration) yielded widespread activation clusters in fronto-parieto-temporal regions bilaterally (Table 7.6). In the LH, it encompassed the IFG pars orbitalis (BA 47), superior frontal gyrus (SFG) pars medialis or the supplementary motor area (SMA, BA 6), the STG (BA 22) and the superior parietal lobe (SPL, BA 7). In the RH activation foci were found in the anterior cingulate gyrus (BA 24), the MTG (BA 21), the SPL (BA 5), the precuneus (BA 7), the lingual gyrus (BA 18) and the cerebellum. At the left side, a large cluster of peri-Rolandic activation extended in an anterior direction over the primary motor and premotor cortex of the precentral gyrus (BA 4/6), and in the posterior direction over the postcentral gyrus (BA 3) (see Figure 7.5). An equivalent, but smaller cluster was visible in the RH, encompassing mainly the postcentral gyrus (BA 3). Importantly, significant activation was also found in the right ventral pallidum (i.e., a subregion of the BG also analyzed in the ROI analysis, see Figure 7.5).

Sentences > CS

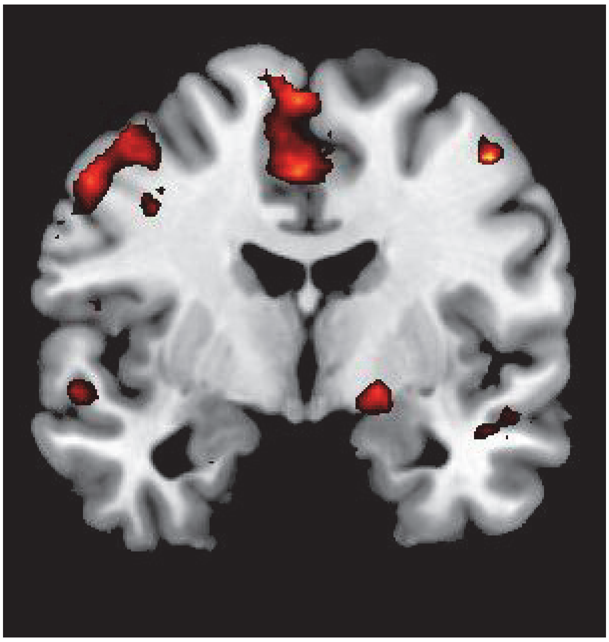


Figure 7.5: Areas activated in whole-brain analysis for reading of sentences in comparison to looking at CS overlaid on a coronal slice of the brain. The results are thresholded at $p < .05$, corrected for multiple comparisons.

Table 7.6: Results of whole-brain analyses comparing reading of sentences versus looking at CS (whole sequence duration)

Region	BA	Side	MNI Coordinates			T-value	k_E
			x	y	z		
SMA	6	L	-8	4	58	8.76	661
Cingulate gyrus	24	R	2	18	40	5.78	96
Post-&precentral gyrus	3/4/6	L	-58	-22	44	8.09	1579
Postcentral gyrus	3	R	54	-24	42	8.04	220
Inferior frontal gyrus	47	L	-44	32	-6	6.48	69
Superior temporal gyrus	22	L	-58	-38	4	8.92	1044
Middle temporal gyrus	21	R	52	-24	-6	6.12	290
Middle temporal gyrus	21	R	54	-2	-16	5.91	100
Superior parietal lobe	5	R	22	-46	68	5.16	81
Superior parietal lobe	7	L	-26	-60	46	5.10	57
Superior parietal lobe	7	R	30	-60	36	6.81	194
Precuneus	7	R	10	-70	34	5.13	94
Lingual gyrus	18	R	12	-88	-2	7.29	468
Ventral pallidum	-	R	18	-4	-8	6.24	72
Cerebellum	-	R	20	-58	-20	5.37	60

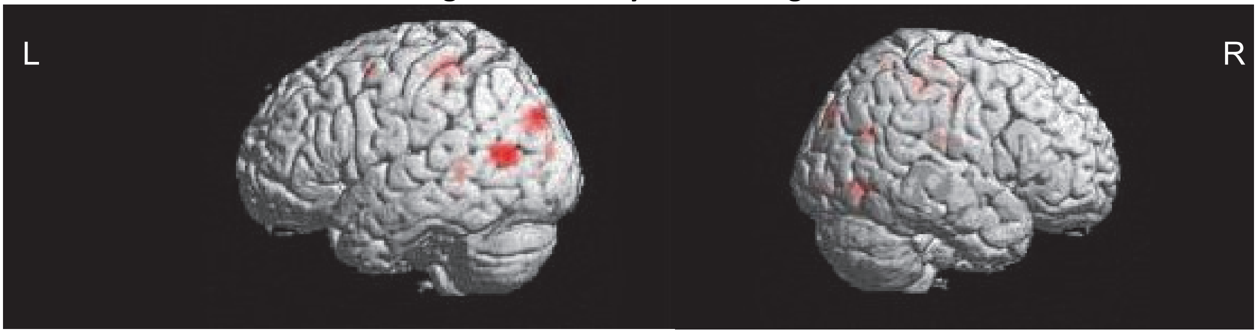
Note: The T-value is of the maximally activated voxel of which the corresponding MNI-coordinates are given. Results are corrected for multiple comparisons at $p < .05$.
For abbreviations see List of Abbreviations.

For the factorial analysis, we first investigated in which regions passive sentences elicited stronger activations than active sentences with a one sample t-test. Increased activation for passive sentences was found in the left lingual gyrus (BA 18, T = 4.91, $p_{corrected} < .05$, peak coordinates -24, -84, -10, k_E = 591). For completeness, we also used a one sample t-test to explore increased activation for active sentences compared to passive sentences. There were no areas which survived the *a priori* set statistical threshold. However, informal inspection at a lower, uncorrected threshold ($p < .05$, uncorrected) showed increased activation in two small clusters of voxels situated in the right Put (i.e., a subregion of the BG also analyzed in the ROI analysis) (T = 3.90, $p_{uncorrected} = .01$, peak coordinates 26, -4, -4, k_E = 43) and the lateral aspect of the left SFG (BA 6, T = 5.04, $p_{uncorrected} = .013$, peak coordinates -20, 6, 62, k_E = 39). The latter cluster is a rostral extension of the dorsal premotor cortex.

Second, we explored the regions that showed differences in activation for the main effect of grammaticality (see Figure 7.6 A and B; Table 7.7). Changes were found in the left SMA (BA 6) and precentral gyrus (BA 6). Also the left MTG (BA 21) was activated. However, the global maximum mapped onto the left posterior MTG (BA 39), and to a lesser extent activation was also found in the right MTG (BA 39).

Another large collection of clusters of activation was identified in the right parietal cortex, with a cluster in (i) the SPL (BA 7) along the posterior extension of the inferior parietal sulcus (IPS), (ii) the inferior parietal lobe (IPL, BA 40) along the anterior segment of the IPS and (iii) the parietal operculum (BA 40). Furthermore, activations of visual processing areas in the occipital lobe were present (see Table 7.7).

A Main effect of grammaticality: left and right lateral view



B Main effect of grammaticality: anterior and posterior view

Figure 7.6: Areas activated in whole-brain analysis to the main effect of grammaticality overlaid on a template brain surface. A: left and right lateral view; B: anterior and posterior view. The results ares thresholded at p < .05, corrected for multiple comparisons.
Note: For abbreviations see List of Abbreviations.

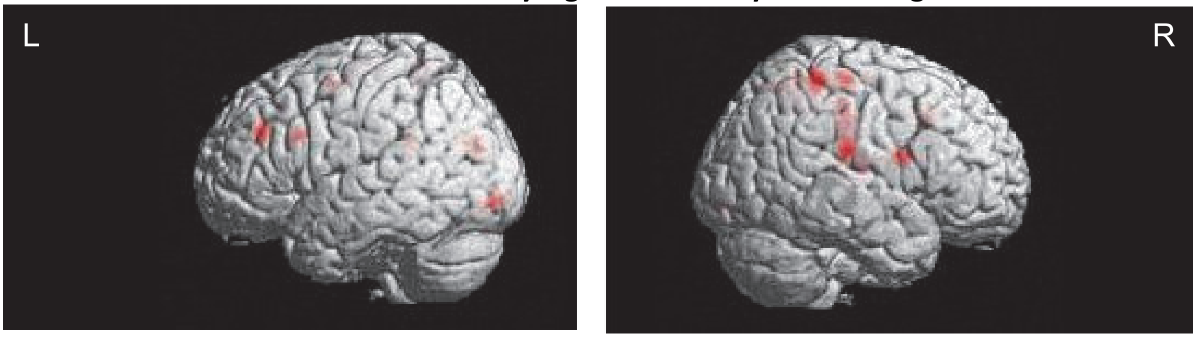
Table 7.7: Activated areas for the main effect of grammaticality

Region	BA	Side	MNI Coordinates			F-value	k_E
			x	y	z		
SMA	6	L	-6	-26	58	12.19	92
Cingulate gyrus	23	R	8	-26	46	11.41	40
Precentral gyrus	6	L	-34	2	56	13.52	21
Middle temporal gyrus	21	L	-68	-44	2	11.45	34
Middle temporal gyrus	39	L	-54	-68	12	21.14	280
Middle temporal gyrus	39	R	46	-66	28	11.20	38
Inferior temporal gyrus	37	R	48	-72	-4	12.04	50
Inferior parietal lobe	40	R	38	-36	48	12.84	60
Parietal operculum	40	R	54	-26	22	11.16	24
Superior parietal lobe	7	R	20	-56	62	12.56	22
Superior occipital gyrus	19	R	16	-88	34	13.37	50
Middle occipital gyrus	19	L	-30	-86	32	19.41	215
Middle occipital gyrus	18	L	-34	-90	14	12.42	26
Calcarine fissure	17	L	-10	-86	0	12.64	57
Inferior occipital gyrus	18	R	20	-90	-6	11.23	23
Fusiform gyrus	19	R	24	-74	-12	11.86	42

Note: The T-value is of the maximally activated voxel of which the corresponding MNI-coordinates are given. Results are corrected for multiple comparisons at $p < .05$, False Discovery Rate, FDR. For abbreviations see List of Abbreviations.

Finally, also the regions whose activation patterns showed significant interactions between canonicity x grammaticality (see Figure 7.7 A and B; Table 7.8) were investigated. Increased activation was found in the bilateral SMA (BA 6) and the IPL (BA 40). The LH the MFG (BA 46) and the lingual gyrus (BA 18) were found to be activated. The interaction effect was also significant in the RH including the ventral premotor cortex (BA 6/44), which is at the junction of the prefrontal and IFG, the MFG (BA 9), and the precuneus (BA 7). Significant recruitment of the right insula for the interaction of canonicity x grammaticality was also observed.

A Interaction effect of canonicity x grammaticality: left and right lateral view



B Interaction effect of canonicity x grammaticality: anterior and posterior view

Figure 7.7: Areas activated in whole-brain analysis for the interaction between canonicity and grammaticality overlaid on a template brain surface. A: left and right lateral view; B: anterior and posterior view. The results are thresholded at p < .05, corrected for multiple comparisons. *Note:* For abbreviations see List of Abbreviations.

Table7.8: Activated areas for the interaction of canonicity x grammaticality

Region	BA	Side	MNI Coordinates			F-value	k_E
			x	y	z		
SMA	6	L	-8	-12	62	11.77	21
SMA	6	R	4	-26	58	12.09	37
Ventral premotor cortex	6/44	R	62	6	18	11.98	47
Middle frontal gyrus	46	L	-40	36	30	16.99	60
Middle frontal gyrus	9	R	30	18	38	15.00	36
Middle frontal gyrus	9	R	48	26	36	13.46	70
Inferior parietal lobe	40	L	-44	-42	24	15.25	22
Inferior parietal lobe	40	R	56	-24	22	12.85	96
Superior parietal lobe	7	R	20	-60	56	12.86	89
Lingual gyrus	18	L	-12	-88	-10	19.99	158
Insula	-	R	42	-16	14	15.74	43

Note: The T-value is of the maximally activated voxel of which the corresponding MNI coordinates are given. Results are corrected for multiple comparisons at p < .05, FDR. For abbreviations see List of Abbreviations.

7.4 Discussion

As set in the introduction of this chapter, the IFG and the BG contribute to sentence processing and the present event related fMRI study investigated the relative contributions of both regions. The sentences were manipulated for canonicity (active or passive voice) in which grammaticality was varied: correct sentences without violation, sentences containing an inflectional violation, or sentences with verb-argument structure violation. Our study suggests that the BG and frontal cortex are differentially involved in processing canonicity and grammaticality. Subparts of the BG complex are mainly involved in processing word order or canonicity (i.e., active versus passive), whereas all the regions of the IFG show more effects of grammaticality, although there is also evidence for an interaction with canonicity.

We identified those areas which are typically involved in language processing in general, from word detection to sentence comprehension, by contrasting reading for comprehension of sentences versus looking at CS: a network of frontal and temporal activations in the LH that are known to be crucial for semantic processing of sentences such as the IFG pars orbitalis (BA 47) and the MTG (BA 22) was evident. However, the CS served primarily as a baseline for identifying relative changes in activation in the six sentence conditions for the factorial analysis. In the following, we will discuss the effect of canonicity and grammaticality in turn.

7.4.1 Effect of canonicity in the right pallidum

In the ROI analysis an effect of canonicity or word order was evident in the right pallidum or GP, in which more activation was found for the active sentences compared to the passive sentences. From the whole brain analysis, two key findings are related to this result. From the subtraction of the activation for processing CS from reading sentences, activation in the right ventral pallidum was also evident. Additionally, when comparing the activation for the active sentences with the passive sentences, the right Put was activated, though this activation was at a low, uncorrected threshold. These findings suggest that the participants activated subnuclei of the right BG the most when processing sentences in which the arguments were in canonical order. That is, although these results suggest that the BG play some role in the processing of canonicity, it is not in response to syntactic complexity per se.

Although language is normally thought to be left-lateralized, the BG activation for active sentences was right-lateralized. Right BG activation seems to be quite typical, especially for tasks requiring selection of one option, or inhibition of a more common alternative. Marangolo and Piras (2008, 2010) and Marangolo et al. (2006), reported involvement of the right BG in derivational morphological processing. BG function was attributed to response selection and inhibition mechanisms required by the derivational task in which participants had to derive a noun from a verb (Marangolo & Piras, 2008, 2010; Marangolo et al., 2006).

Using semantic priming experiments, Copland and colleagues (Copland 2003, 2006; Copland et al., 2000, 2001) have demonstrated the importance of particularly the right striatum in ambiguity processing. Examining syntactic ambiguity, Stowe et al. (2004) found right Caud involvement and explained this as inhibition of the irrelevant possibility based on later context, thus ‘unchoosing’ the initially selected structure. Recently, Snijders et al. (2009)

reported a similar effect of ambiguity in the right striatum. As a follow up, Snijders et al. (2010) examined how the striatum is functionally connected to cortical language areas while processing word-category ambiguity. Particularly for sentence-ambiguous versus sentence-unambiguous conditions, the striatum was connected to left and right MTG and LIFG; this pattern was not found in word list contexts where no choice has to be made.

In the ROI analysis of the current study, we found a striking effect of word order in the right pallidum rather than the right striatum and for the more likely active structure rather than the less likely passive. Thus, the locus of the effect is not the subnuclei which receive input (i.e., the striatum) but rather the output subnucleus. The pallidum receives corticostriatal inputs and projects back to discrete frontal regions via the thalamus, closing the cortico-striato-cortical circuit. The activation of the right pallidum is consistent with activation found during tasks investigating performance on cognitive tests of planning and visual spatial working memory (WM) (Owen et al., 1998).

Based on the current knowledge of BG function, one possible explanation for this activation is that the BG play a role in encoding word order information comparable to their role in building goal-oriented action sequences (Graybiel, 1995a, 1995b; Graybiel et al., 1994), by establishing syntactic, thematic relations and semantic relations (Friederici, 1995, 2002). Healthy individuals are known to primarily use simple heuristics to process sentences in addition to the more time-consuming syntactic algorithms (e.g., Ferreira, 2003), including the tendency to assume that the subject of a sentence is the agent of the action and the direct object is the patient (Townsend & Bever, 2001). The BG are perfectly located for such a role in facilitating heuristic strategies, because they are closely interconnected with the frontal cortex via the cortico-striato-cortical circuits (e.g., Alexander et al., 1986). Saint-Cyr (2003) stated that for consciously selected goals, awareness of the environment and identification of salient cues, the ‘supervisory attentional system’ or SAS is responsible, which must be attributed to the cortex. However, context may be implicitly encoded by the BG, so that the context recognized by the cortex may cue the striatum to evoke dopamine-potentiated rules (Wise et al., 1996). Subsequent simultaneous transmission trough the direct and indirect pathways leads to the selection of frequently successful (rewarding) activation patterns in the output structures, which facilitate processing routines in the frontal cortex. This suggestion is based on the model for selecting goal-directed actions, and may be particularly applicable because transitive active sentences frequently represent actions.

To sum up, activation of the right GP in the participants in our experiment makes it clear that this part of the BG plays a role in the processing of constituent order during sentence comprehension, which could reflect facilitation of heuristic routines during sentence comprehension. Moreover, this finding supports contribution of the right GP instead of the more frequently reported striatum to sentence comprehension, but in response to a clearly different aspect of response selection.

7.4.2 Effect of grammaticality in the inferior frontal gyrus

The results of the ROI analysis showed that activation in the IFG clearly is influenced by the factor of grammaticality on its own or in interaction with canonicity. The overall pattern for the ROIs was that the well-formed sentence was more activated than the violated sentences, particularly the sentence with a violation of the verb-argument structure (e.g. * Emma heeft de vlinder geniesd, *'* Emma has the butterfly sneezed'*). This pattern was seen as a trend to a main effect for the bilateral pars orbitalis (BA 47) and pars triangularis (BA 45). In the BA 45, the effect was larger for the RH. Furthermore, it is clear that grammaticality and canonicity interacted in both the BA 44 and BA 45, with larger effects of violation for the active sentences than the passive sentences.

As discussed in the introduction, in a variety of morphosyntactic violation tasks using functional neuroimaging, activation of subregions of the IFG has been found (Kuperberg et al., 2000, 2003; Moro et al., 2001; Newman, et al., 2001; Newman, et al., 2003; Ni et al., 2000; Raettig et al., 2010; Ruschemeyer et al., 2005). Kuperberg et al. (2003) found results similar to ours, possibly because they used simple active sentences. In their study, the BA 47 showed more activity in association with the normal sentences, and less activity in association with morphosyntactically anomalous sentences. More recently, on the other hand, Raettig et al. (2010) found a strong activation in left BA 44 for violation of the verb-argument structure relative to no violation. Possible explanations for this difference might be 1) their exclusive use of the passive voice, which also showed a trend in this direction in our data, 2) the grammaticality judgment task employed or 3) other methodological differences with the present study. However, the discussion of these differences is beyond the scope of the current study.

Three ROIs in the bilateral IFG were included in the analysis in order to follow up suggestions in the literature that processing within the IFG varies along a posterior/dorsal to anterior/ventral gradient (Friederici, 2002; Hagoort, 2003, 2005; Hagoort et al., 2004). According to these researchers, more posterior subregions (BA 44/45) contribute to morphosyntactic processing, while more anterior subregions (BA 45/47) are involved in semantic processing. Several neuroimaging studies have supported this distribution of functional specialization tied to semantic and syntax processing within the IFG (e.g., Friederici et al., 2000, 2003; Meyer et al., 2000; Ni et al., 2000). Consistent with the claim on functional specializations within the IFG, in the present study interaction with word order was found in the more posterior superior regions (BA 44/45), while the anterior inferior regions (BA 45/47) were mainly sensitive to violation, particularly violation of the verb-argument structure.

Additionally we wished to further investigate the role of the RH in violation processing. Meyer et al. (2000) reported involvement of the right BA 45 during the processing of violations (i.e., main grammaticality effect). However, in the Meyer et al. (2000) study, activation in the right BA 45 was detected primarily when participants performed a repair task on syntactically incorrect sentences and for a rather different set of violations. The pattern of results which we see is not compatible with repair, as they suggested, but might involve additional integration in well-formed sentences (Bookheimer, 2002).

7.4.3 Effects of canonicity and/or grammaticality in other areas

Processing active sentences was associated with increased activation compared to passive sentences in the lateral aspect of the left BA 6 and the right Put in the whole brain analysis. The network of areas showing effects of grammaticality consisted of the following areas: the left BA 6, the right parietal cortex, the left BA 21 and the right BA 37.
The posterior ventral premotor cortex (BA 6), which showed increased activity for active sentences in this study, is most basically involved in motor planning. According to sensory-motor theories of conceptual knowledge, sensory-motor information about actions is not only accessed during the comprehension of perceived actions but also during the comprehension of action words (Martin & Chao, 2001; Pulvermüller, 2005; Rizzolatti et al., 2001). BA 6 has also been found to be related to representations of abstract sequential order (Schubotz & Von Cramon, 2002; 2004). Combining these concepts, Den Ouden et al. (2009) reported frontal activations similar to those found in our study and concluded that the lexical representation of a verb distributed within the BA 6 contains information on the goal direction of the action and its argument structure. Since basic word order characteristic for active sentences follows the direction of the action represented in the lexical representation of the verb, the present results may be related the processing of basic action order representation in active sentences. The right pallidum activation may also be interpretable within this framework, in which referring to goal directed action uses many of the same underpinnings as planning motor sequences.

Turning to the activations found for grammaticality, the increased activation of one part of the parietal cortex (i.e., right IPS) is similar to the activations found in violation studies by Bornkessel et al. (2005) and by Kuperberg et al. (2003). The right SPL has been suggested to be involved in short term storage implicated in WM (Otsuko et al., 2008). WM is involved in the temporary storage and processing of information, which supports higher cognitive functions such as sentence comprehension. In the original multicomponent model of Baddeley (1986), domain-specific (verbal and visuo-spatial) short-term storage buffers act to maintain information, whereas the central executive system manipulates the information held in these buffers. During the performance of the reading span test, Otsuka et al. (2008) found bilateral but stronger right-hemispheric activity of the SPL in older participants, whereas the young showed unilateral (left) activation. It was therefore concluded that the right SPL is associated with short-term storage rather than executive function of WM in the elderly. Our findings are consistent with this claim.
The right precuneus (BA 7) was also activated for the interaction effect of canonicity and grammaticality. The precuneus has been associated with visuo-spatial imagery, episodic memory retrieval and self-processing operations (Cavanna & Trimble, 2006), but was also activated in response to more language related characteristics of stimuli like anomalous word order (Moro et al., 2001), the number of verb complements (Shetreet et al., 2007; Den Ouden et al., 2009) and in response to verbs with lower imageability (Shetreet et al., 2009). Activation of the precuneus in the present study might thus be related to the processing of lexical information of high complexity.

It is important to point out that contrary to the conclusions from lesion data, neuroimaging data like ours illustrate that the processing of morphosyntactic violations may involve temporal lobe structures and that certain lexical-semantic functions appear to depend upon frontal regions.

7.4.4 Future studies

A large number of neuroimaging studies have investigated the effects of canonicity and grammaticality separately, while interactions between these two aspects of language have not received much attention. The current study therefore tested both aspects of language. In addition, the current data suggest that the wrong generalization can be made if only active or only passive sentences are used. However, violated sentences may recruit controlled processes not engaged by normal sentence processing at all, such as violation detection and violation repair, even if this was not explicitly asked from the participants. The behavioral data support this idea: we see faster RTs for the non-violated condition in comparison to the violated conditions, suggesting that successful completion of this condition probably required less attentional effort than both violated conditions.

Furthermore, additional research is indicated to confirm the differential role of the BG and IFG in sentence comprehension.

First, in the future, the question of the connectivity between the IFG and BG needs to be answered more in depth. Therefore, either a DTI study would need to elucidate the existence of a structural based white matter network between the regions or a functional connectivity analysis would have to provide functional evidence for a BG-frontal cortical network during the comprehension of sentences in which the variables of canonicity and grammaticality are crossed. A connectivity analysis is planned in the near future.
Secondly, the involvement of the pallidum reported here possibly explains the deficit in comprehension of non-canonical sentences in PD patients. PD comprehension deficits may be caused by a disruption of BG outflow resulting in frontal dysfunction in the circuit connecting the IFG and BG (Snijders et al., 2010; Ullman, 2006). In the next chapter of this thesis, the question whether PD patients demonstrate a lack of activation of the subparts of the BG-frontal cortical network during sentence processing is answered.

7.5 Conclusions

To conclude, the results of this fMRI study suggest a distinct role for the IFG and BG, which are in a highly complex relationship with each other, with major contributions to distinct aspects of comprehension. We suggest that the BG play a significant role in the processing of basic word order. By contrast, the right BA 45 and the bilateral BA 47 (to a lesser extent), are mainly involved in the higher-level semantic processing of well-formed sentences. Our findings furthermore demonstrated that right-hemispheric activation was prominent in the healthy seniors tested. It should be noted, however, that the BG interact with the cerebral cortex through a complex series of loop circuits. Intact BG may be important to get the activations we see in the IFG, without itself showing the same pattern.